UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/742,346	12/19/2003	Robert Falotico	CRD-5062 USANP	6421

27777 7590 07/24/2008

PHILIP S. JOHNSON
JOHNSON & JOHNSON
ONE JOHNSON & JOHNSON PLAZA
NEW BRUNSWICK, NJ 08933-7003

EXAMINER	
HELM, CARALYNNE E	
ART UNIT	PAPER NUMBER
1615	
MAIL DATE	DELIVERY MODE
07/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/742,346	FALOTICO ET AL.	
	Examiner	Art Unit	
	CARALYNNE HELM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 2, 2008 has been entered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-7, and 9-10 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Tseng et al. (Pregrant Publication No. US 2005/0065596 A1) in light of Windecker et al. (Current Pharmaceutical Design) and Roorda et al. (US. PGPub No. 2005/0106203).

In claim 1, Tseng et al. teach a stent (an implantable structure), containing drug depots capable of controllably delivering one or more histone deacetylase (HDAC) inhibitors (see instant claims 6-7). In addition, Tseng et al. also teach that the disclosed device delivering the HDAC inhibitors is particularly beneficial in the treatment of restenosis, implying that the HDAC inhibitors would be present at therapeutic dosages within the stent device (see paragraph 37; instant claim 6). Tseng et al. go on to further describe the HDAC inhibitor included on or in the

stent body as trichostatin A, abbreviated as TSA (see claims 12-14 and paragraph 15 lines 1-2; instant claim 9). Also taught by Tseng et al. is the inclusion of an additional pharmaceutical agent or agents, such as anti-inflammatory and anti-proliferative agents, where an exemplary agent includes rapamycin (see paragraph 134 lines 1-4 and 12-13 and claims 2 and 3; instant claim 6). Tseng et al. does not specifically teach rapamycin as the preferred additional pharmaceutical; however, Windecker et al. teach that rapamycin (also known as sirolimus) has powerful anti-proliferative and anti-migratory drug properties on vascular smooth muscle cells (see page 1089 column 1 paragraph 1 lines 1-5; instant claim 10). In addition, Windecker et al. go on to teach that its incorporation into biocompatiable polymers, suitable for stent based drug delivery, has been successful (see page 1089 column 1 paragraph 1 lines 5-7; instant claim 10). One of ordinary skill in the art at the time of the invention, would have found it obvious to couple the device of Tseng et al. with the teachings of Windecker et al. to produce a stent (an implantable medical device) containing drug depots capable of controllably releasing therapeutic dosages of trichostatin A and rapamycin, an anti-proliferative. Tseng et al. teach that the drug depots include one or more polymers (see claim 6), but do not specifically describe the polymer-drug configuration as a coating on the stent device.

Roorda et al. teach a drug eluting stent with drug-polymer base layer and an additional polymer topcoat (see paragraph 12 lines 1-4; instant claim 6). Roorda et al. go on to teach that the topcoat serves as a rate limiting membrane to control the release of drug from the device (see paragraph 12 lines 8-11; instant claim 6). Roorda et al. teach that these coating layers are composed of polymers and that both polyacrylates alone and in conjunction with fluorinated polymers are considered suitable varieties (see paragraph 28 and 29 lines 1-3; instant claim 6). Further, Roorda et al. teach a configuration where poly(n-butyl methacyrlate) is used as a topcoat and in a blend with another polymer in the drug containing layer (see paragraph 29 and

example 18). One such other polymer is taught to be a fluorinated polymer, namely poly(vinylidene fluoride-co-hexafluoro propene) (see paragraph 28). This copolymer is exemplified in use as a coating on the device where the proportion of vinyldiene fluoride to hexafluoro propene is 85:15 (see example 12). Differing polymer properties and associated drug release kinetics are achieved as the proportion of the monomer in the polymer backbone of the coating is varied. Various amounts of poly(n-butyl methacrylate) are taught to be included in the topcoat including 200 μg and 300 μg. Since the amount of polymer present in the topcoat has a controlling effect on the rate of release of the contained drug, it would have been obvious to one of ordinary skill in the art to optimize this quantity to achieve particularly desired release kinetics. The reference does not teach the particular claimed vinyldiene fluoride to hexafluoro propene ratio in the copolymer or amount of poly(n-butylmethacrylate) present in the topcoat. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such parameters as a matter of routine experimentation and achieve the claimed values.

The applicant teaches in the instant specification that any combination of fluoropolymer and acrylics would produce incompatible polymer chemistry, therefore the described coating formulations of Roorda et al. would have the claimed characteristic of immiscibility (see instant specification page 127 lines 11-15 and claim 6). A person of ordinary skill in the art at the time of the invention would have found it obvious to use the coating configuration of Roorda et al. to produce the device taught by the Windecker et al. modified Tseng et al. invention where an antiproliferative (rapamycin) and a HDAC (trichostatin A) inhibitor are located in a basecoat polymeric material to which a topcoat polymeric material is attached and where the two layers are composed of immiscible polymeric material. Since all three inventions address the issue of the body's response to medical device implantation (drug eluting stents) one skilled in the art

would have had a reasonable expectation of success for the combination. Thus, claims 6-7, and 9-10 are obvious over Tseng et al. in light of Windecker et al. and Roorda et al.

Claims 6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tseng et al. in light of Carter et al. (US Pregrant Publication No. US 2002/0013616 A1), Windecker et al. and Chudzik et al.

As previously described Tseng et al. modified by both Windecker et al. and Roorda et al. teach a stent device with drug depots containing trichostatin A and rapamycin, where the drugs are contained within a polymeric basecoat and are able to be controllably released in therapeutic dosages, and further contains a polymeric topcoat that controls the drug elution and whose polymer is immiscible with that of the basecoat (see ***Claim Rejections - 35 USC § 103*** of claims 6-7 and 9-10 above). The modified Tseng et al. reference also teaches that the reasoning for incorporating the trichostatin A, the HDAC inhibitor, within the stent device is for dealing with the issue of restenosis following stent implantation (see Tseng et al. paragraphs 29, 31, and 37). Tseng et al. modified by Windecker et al. and Roorda et al. does not specifically teach stent grafts containing the drug depots with controllable release capabilities. Carter et al. teach that stents are commonly used to clear obstructions and to repair damage to vascular tissue (see paragraph 39 lines 2-5). Carter et al. go on to teach that stent grafts are a common name for a modification of stents where a flexible covering is attached to the stent frame (see paragraph 39 lines 10-12) and that the implantation process for stents, as a whole, carries with it the risk of causing restenosis (see paragraph 50 line 9). Since stent grafts are a modification of stents and also subject to post-implantation restenosis, it would have been obvious to one skilled in the art at the time of the invention to further modify the invention of Tseng et al. in light of Windecker et al. and Roorda et al., by incorporating the controllably releasing drug depots,

configured as a bilayered polymeric coating containing trichostatin A and rapamycin, within a stent-graft device. Therefore, instant claim 8 is obvious over Tseng et al. in light of Windecker et al., Roorda et al., and Carter et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-8 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8, 9, 10, and 12 of copending Application No.10/805,736 in light of Pribluda et al. (Cancer and Metastasis) and Roorda et al. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant application claims a medical device comprising an implantable structure, both a histone deacetylase (HDAC) inhibitor and an anti-proliferative, specifically rapamycin, in therapeutic dosages releasably affixed to the structure, for the treatment of restenosis (see instant claims 6 and 10). This recitation by the applicants broadly includes all implantable

structures, such as a biocompatible implantable structure, as well as the rapamycin claimed in application '736. In addition claims 9, 10, and 12 further limit claim 8 of application '736 in exactly the same fashion as instant claims 7 and 8 further limit instant claim 6. Application '736 does not specifically teach the use of a HDAC inhibitor or a topcoat–basecoat configuration such that the polymers in each are immiscible. The HDAC inhibitor has the property of inhibiting cellular proliferation (see Tseng et al. paragraph 121 lines1-4). Pribluda et al. teach that 2-methoxyestrdiol also has the property of inhibiting cellular proliferation (see page 173 column 2 paragraph 1 lines 1-8). One skilled in the art at the time of invention would have found it obvious to exchange one anti-proliferative drug for another in the instant application, namely use 2-methoxyestradiol instead of the HDAC inhibitor in the medical device. Although claimed in general, application '736 does not teach a particular fluoropolymer or acrylic polymer. However in view of the teachings of Roorda et al. it would have been obvious to use poly(n-butyl methacrylate) as the acrylic polymer topcoat and poly(vinylidene fluoride-co-hexafluoride propene) as the fluoropolymer (see paragraphs 28-29 and table 1). It would also be obvious to employ these polymers at the claimed levels based upon further teachings by Roorda et al. (see ***Claim Rejections - 35 USC § 103*** of claim s 6-7 and 9-10 above). As both the instant invention and that of Roorda et al. seek to controllably release drug form an implantable device it would have been obvious to one of ordinary skill at the time of the invention employ the particular polymers taught by Roorda et al. in the invention of application '736. Therefore, instant claims 6, 7, 8 and 10 and 11 are provisionally rejected as being unpatentable over claims 8, 9, 10, and 12 of application 10/805, 736 in light of Pribluda et al. and Roorda et al.

Claims 6-8, and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, and 10-11 of copending

Application No.10/796,397 in light of Waksman (Cardiovascular Radiation Medicine), Hardman et al. (Goodman and Gilman's: The Pharmacological Basis of Therapeutics), and Roorda et al. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant application claims a medical device comprising an implantable structure, both a HDAC inhibitor and an anti-proliferative, specifically rapamycin, present in therapeutic dosages, releasably affixed to the structure for the treatment of restenosis following vascular injury (see instant claims 6 and 10). Waksman teaches that the pathology of restenosis involves the hyper-proliferation of cells and matrix synthesis, elastic recoil (when balloon angioplasty has been employed), and late vascular contraction resulting in a decrease in vessel diameter (see page 226 column 2 paragraph 1 lines 5-11). Waksman goes on to teach that strategies for preventing restenosis have focused on anti-proliferative therapies and intervention into the cell cycle (see page 227 column 1 paragraph 1 lines 5-9). Topoisomerase I inhibitors interfere with the cell cycle by blocking the religation of DNA that is ordinarily facilitated by topoisomerase and ultimately results in cell death (see Hardman et al. page 1423 column 1 paragraph 2 lines 8-9 and paragraph 3 lines 1-10). This interference in the cell cycle focuses on the S-phase for eliciting its cytotoxic effect (see Hardman et al. page 1423 column 1 paragraph 3 lines 10-12). The invention of instant claims 6-8 and 10 contains all the limitations of the invention in claims 1-7, and 10-11 in application '397, except that the instant application uses trichostatin A, a HDAC inhibitor, instead of a topoisomerase I inhibitor. Since it has been established in the art that targeting both proliferation and the cell cycle are viable strategies for treating restenosis, one of ordinary skill in the art at the time of the invention would have found it obvious to replace the topoisomerase I with a HDAC inhibitor, in effort to treat the causes of restenosis. Although claimed in general, application '397 does not teach a particular fluoropolymer or acrylic polymer. However in view of the teachings of Roorda et al. it would have been obvious to use poly(n-butyl

methacrylate) as the acrylic polymer topcoat and poly(vinylidene fluoride-co-hexafluoride propene) as the fluoropolymer (see paragraphs 28-29 and table 1). It would also be obvious to employ these polymers at the claimed levels based upon further teachings by Roorda et al. (see ***Claim Rejections - 35 USC § 103*** of claim s 6-7 and 9-10 above).Therefore, instant claims 6-8, and 10 are provisionally rejected as being unpatentable over claims 1-7, and 10-11 of application 10/796,397 in light of Hardman et al. and Waksman. And Roorda et al.

Claims 6-8 and 10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 8-10 of copending Application No. 10/805,722 in light of Hardman et al. and Roorda et al. The same reasoning presented in the preceding paragraph holds true in the comparison of instant claims 6-8 and 10 with claims 1-6 and 8-10 of application '722. In this instance, instead of a HDAC inhibitor, as is used in the instant invention, application '722 uses a cytostatic glucoside. The specific cytostatic glucosides claimed in '722 are epipodophyllotoxins (teniposide and etoposide) or podophyllotoxins (podofilox), which both interfere with the cell cycle, but act via difference mechanisms; namely, each group of drugs cause cell death through DNA strand breakage or the arrest of cells in mitosis (see Hardman et al. page 1423 column 2 lines 1-10). It has been established in the art that targeting both proliferation and the cell cycle are viable strategies for treating restenosis, thus, one of ordinary skill in the art at the time of the invention would have found it obvious to replace the cytostatic glucoside with a HDAC inhibitor, in effort to treat the causes of restenosis. Although claimed in general, application '722 does not teach a particular fluoropolymer or acrylic polymer. However in view of the teachings of Roorda et al. it would have been obvious to use poly(n-butyl methacrylate) as the acrylic polymer topcoat and poly(vinylidene fluoride-co-hexafluoride propene) as the fluoropolymer (see paragraphs 28-29 and table 1). It would also be

obvious to employ these polymers at the claimed levels based upon further teachings by Roorda et al. (see ***Claim Rejections - 35 USC § 103*** of claim s 6-7 and 9-10 above).Therefore, instant claims 6-8 and 10 are provisionally rejected as being unpatentable over claims 1-6 and 8-10 of application 10/805,722 in light of Hardman et al. and Roorda et al.

The preceding are provisional obviousness-type double patenting rejections because the conflicting claims have not in fact been patented.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CARALYNNE HELM whose telephone number is (571)270-3506. The examiner can normally be reached on Monday through Thursday 8-5 (EDT).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Caralynne Helm/
Examiner, Art Unit 1615

/MP WOODWARD/
Supervisory Patent Examiner, Art Unit 1615